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MSMLAERRRKQKWAVIDPONTAWSNDDSKFGQRMILEKMGWSKGKGIGAQEQQGATDHIRVQ
VKNNHLGLGATINNEDNWIAHODDFNQQLAELINTCHGQETTDSSDKKEKKSF'SLEERSK
ISKNRVRVHVKMFKFTKGKDLSRSKTDLDCIFGKRSKKTPEGDASPSPEENET'TTSAFT
IQEYFAKPVAAALKNKPQVFPVGSDISETOVERKRGKRNKEATGKDVESYTLQPKAKRHT
EGKPERAEAQERVAKKKCAPAERQLRGPCWDQSSKASQDAGDHVQPPEGRDFTLKPKK
RRGKKKLQKPVETIATLEETIVKKKKDSK(328)

FIG. 1A

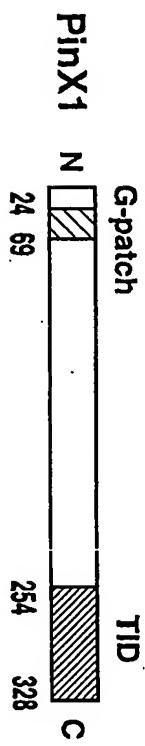


FIG. 1B

HsPinX1 M S M L A E R R K O K W A V D P O N T A W S N D D S K F G Q R M L E K M G W S K G K G L G - A Q E
 CεPinX1 M S I L A E P K R K O K I S I D P O N L T W K N D D Q K L S K K L M E K M G W S E G D G L G - R N R
 ScPinX1 M G - L A A T R T K O R F G L D P R N T A W S N D T S R F G H Q F L E K F G W K P G M G L G L S P M

 O G A T D H I K V O V I K N N H L G I G A - - - T - - I N N E D N W I A H Q D D F N O L L A E L N
 O G N A D S V K I L K A N T S G R G L G A - - - D K M A D Y D S T I S H H D D F A D U L A L N
 N S N T S H I K V S I K D D N V G L G A K L K R K D K K D E F D N G E C A G L D V F O R I L G R L N

 T C H G O E T T D S S D K K E K K S - - F S L E E K S K I S K N R - - V H Y M K F T K G K D L S S R
 S D S H K K G I L G Y G R L K S D N A E E K I S I E L K S K S T I R R R - - T H Y Q F T R A K D T S N Y
 W D P K T H K L R N Y S N A K K R - - - - K R E G D D S E D E D D D K E - - F V R G E V L A S T

 T T - S A F T I Q E Y F A K P V A A L K N K P O V P V P G S D I S E T O V E R K R G K K R N K E A T
 N T V S T L S V G D Y F A A K M A A L K A K R E A A A N - - - Q T E V K M E I K T E V E E E

 G K D V E S Y L Q P K A K R H T E G K - P E R A E A Q E R V A K K C A P A E K O L R G P C W D Q S
 E S D E E - - - K A R R K A E K K E R K R I R R E Q R D K E E T L E T V E T I L - - - E V K
 D K K K D K - - K D K K E H K K K E E K R I K E K R A E K T K E T K K T S K L K S S - - -

 S K A S A Q D A G D H V Q P P E G R D F T L K P K R - - R G K K K L O K P V E I A E D A T L E E T
 Q E V K E E I I D E E F D E A E R K R L K - K E K K R K R L R E Q Q O P E N E G A E G G E A D E E
 F M I T N - - - E S A S N I P D A V N T R L S V R S K - W I K O K R A A L - - - M D S K A L N E I

 L V K K K K K K - - D S K (328)
 E I P R K R K K H T E D E H (339)
 F M I T N - - - D - - (271)

FIG. 1C

GCAGGAATTGGCACGGCTCCAGCCCCCAGTCACCCAGGTCCAGGGC
GGCGGTATCACAGGCTCTCCGACATGTCTATGCTGGCTAACGTCGGGGAGCAGAGTG
GGCTGTGGATCCTCAGAACACTGCCTGGAGTAATGACGATTCCAAAGTTGGCCAGCGGGATG
CTAGAGAAGATGGGGGGTCTAAAGGAAGGGTTAGGGGCTCAGGAGCAAGGAGCCACA
GATCATATTAAGTCAAGTGAATAACCACCTGGGAACTCGGAGCTACCATCAATAATGAA
GACAACGTGGATTGCCATCAGGATGATTAAACCAAGCTCTCGGACAAGAAGGAAAGAAATCTT
TGGCAGGAAACCACAGATTCCAGGAAACTGAAACACTTGCCCTTGAGGAA
AGTCCAAATCTCCAAAACCGGTGTTCACTATGAAATTCAAAGGGAAAGGATCTGTCA
CTCGGAGCAAAACAGATCTGACTGCATTTGGAAAGACAGAGTAAGAAGACTCCCGAG
GGCGATGCCAGTCCTCCACTCCAGAGGAGAACGAAACACCGACCAACCAGCGCCTCACCA
TCCAGGGAGTACTTGCCAAGCCGGTGGCAGCACTGAAGAACACAAGCCCCAGGTTCCAGTCC
AGGGTCTGACATTCTGAGACGCAGGTGGAACGTAAGGGGAGAAAGAAATAAGAG
GCCACAGGTAAGATGTGGAAAGTTACCTCCAGGCTTAAGGCCAAGGGCACACGGGGAA
AGCCCGAGAGGCCAGGCCAGGGAGCTGGCCAGTGGCAAGAAGAAGTGCAGGCCAGCAGAA
AACAGCTCAGAGGGCCCTGCTGGGACCCAGAGTTCCAAGGGCCTTGCTCAGGATGCAAGG
GACCAGTGTGCAGCCGCTGAGGGCCGGACTTACCCCTGAAGCCCAAAAGAGGGAGGG
AAGAAAAGCTGCAAAACCACTAGAGATAGCAGAGGACGCTACACTAGAAGAACGCTAG
TGAAAAGAAGAAGAAGATCCAATGAATCCTTCCAGGGGGCCTCCGACACT

FIG. 1D-1

FIG. 1D-2

FIG. 1D

CAGCTGTCAGGGCACTGCGGGGAGACACCTCTGGCTGAAGTCACGAGAGTCACC
CCAGAGCCCTGGCGCATCTGGCATGCCCATGGGCTGCCGAGTCCTGCCCTCTGC
CACATTCCCCAAGTTACATCCAGGAGACCTTTAATGTTCTCAATCGTGGCTCTCAG
ACACAATAATTCTCGTGCAGAATTGGCACGAGCTCGCTCTCATTCCTGATGTGGACATC
GACTCCGAGGGCGTCTCAAGTATGTGTGATCCGGAGTCCACTCGGACTCCCCGCTCCGGG
CTCCGGCTGCAGAGCAAGGAGATCGTGCCGGCTACAAGGGCTGAGTACCATGCGG
ACATCTACGACAAGTGTGGGAGCATGCAGAAGCAAGGACTGCGACTGTGAGTGTCTGG
CGCGGGGCATCTCCCACCAAGAGTCAGGACAAGAAGATTCACGTGTACGGCTATTCCATG
GCCTATGGTCTGCCAGCACGCCATTCAACTGAGAAATCAAAGGCCAGTACCCGACTA
CGAGGTCACTGGGCTAACGACGGCTACTGGAGCACTCCCAGCCGGGGCCTGTGCTCC
AGCAGCCACTTCAGAGCCCCGCCCTTGCCCTGCACTCCTCTTGCAAGGCTGGCCCTGCTG
CTCCTGCCAGCCTCTGGTGACGTACTGTCCACCAAGGGCTGGAGACAGGCTAGCCTGG
CCACAGAATTAAACGTTGTGCCACACCAAAAAAA

coding regions: 84 to 1070

Protein sequence:

MSMLAERRKQKWAVIDPQNTAWSNDDSKFGORMLKEKMGWSKGKGLGAQEQGATDHIKVQVKNHNLGATTI
NNEDNWIAHQDDFNQLLAELNTCHQGETTDSSDKKEKSFSLEEK3KISKNRVRHMKFTKGDLSSRSKTD
LDCIFGKRSKKTPEGDASPSTPEENETTTSAFTIQEYFAKPVALNKPOVVPVPGSDISETOVERKRKG
KRNKEATGKDVESYLQPKAKRHTEGKPERAEAQERVAKKKCAPAEKQLRGPCWDQSSKASAQDAGDHWQPP
EGRDFTLKPKKRGLQKPVIAEDATLETLVKKKKDOSK

FIG. 1D-2

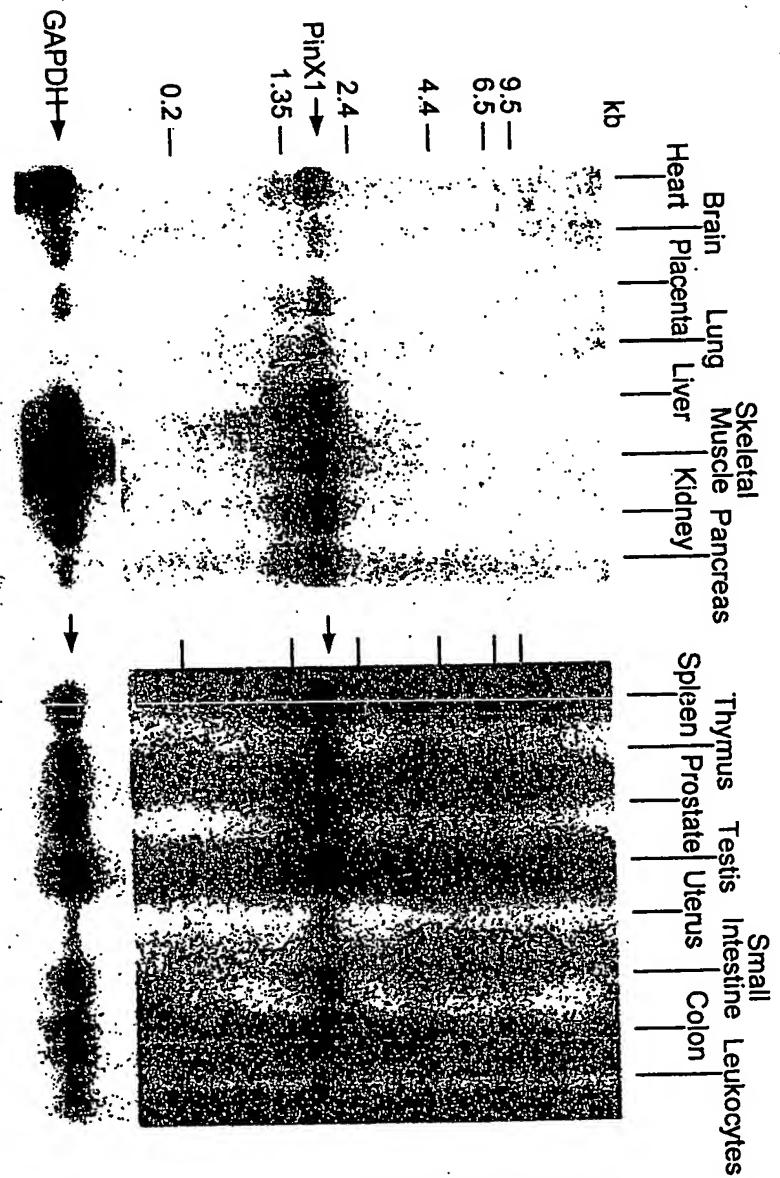
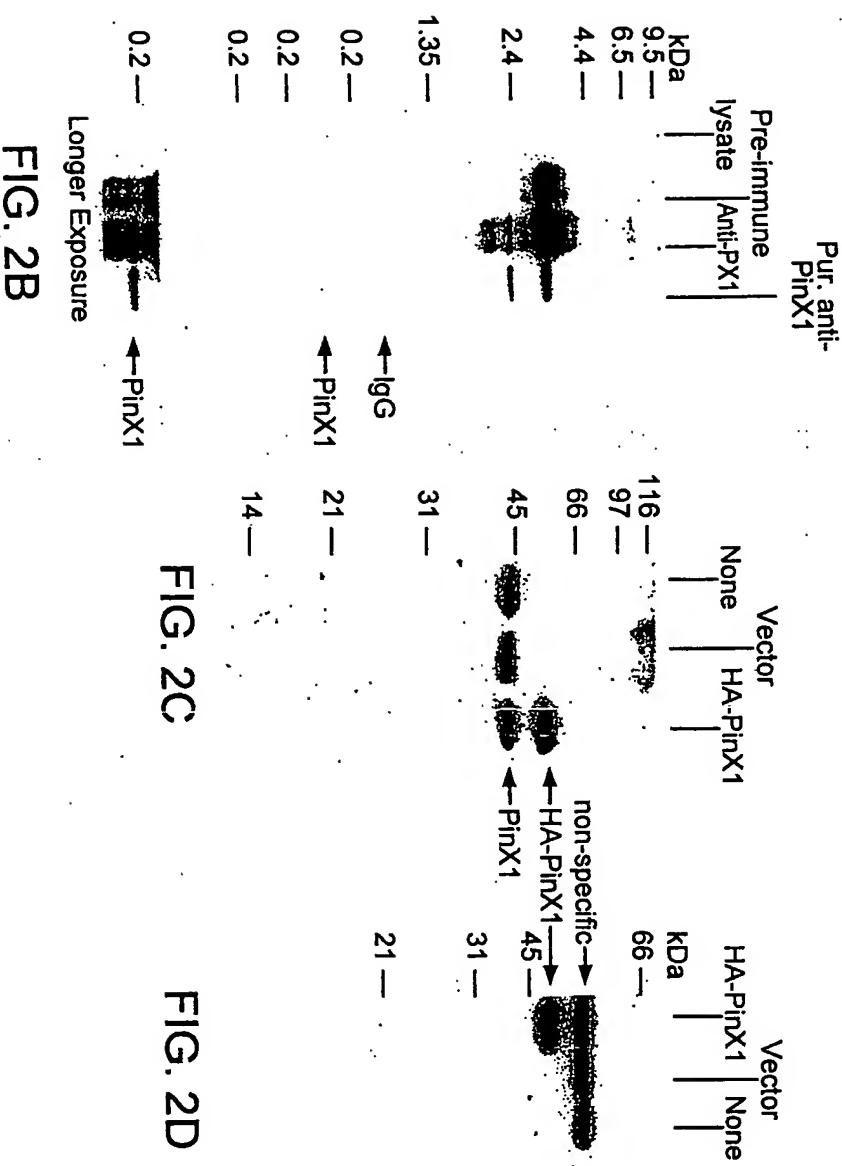


FIG. 2A



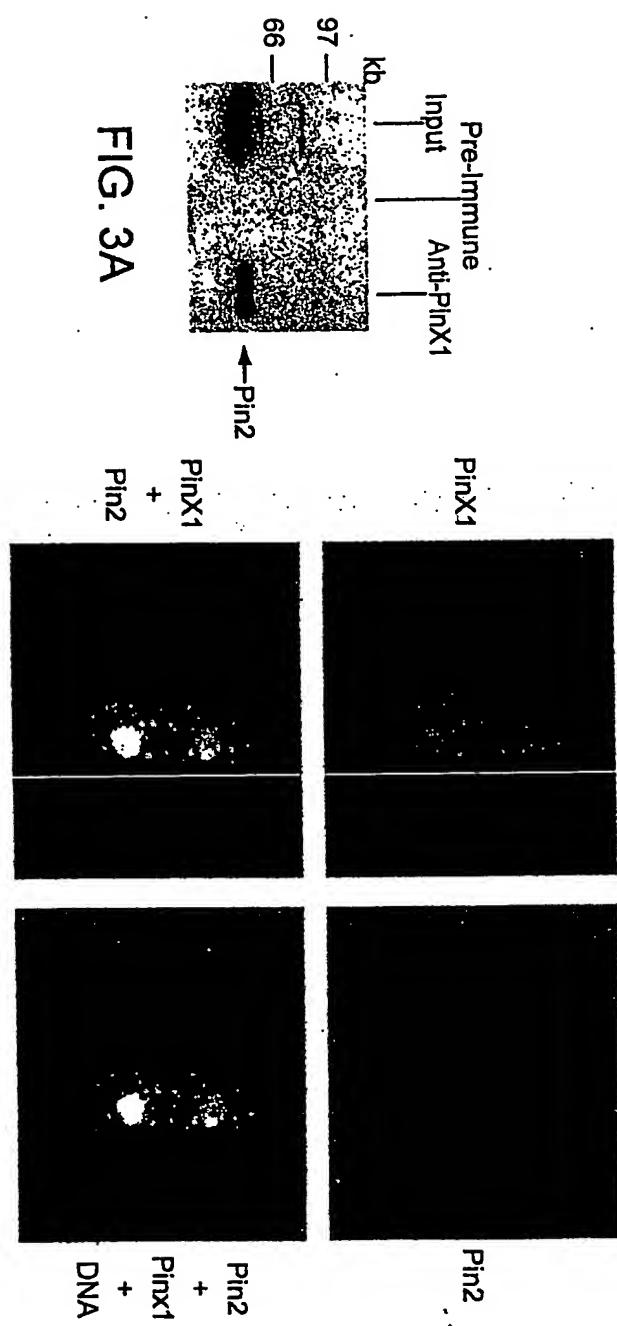


FIG. 3A

FIG. 3B

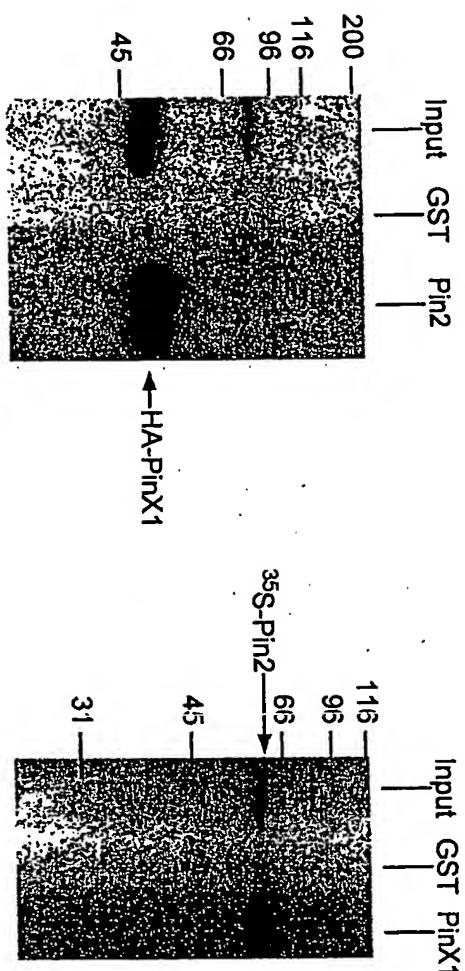


FIG. 3C

FIG. 3D

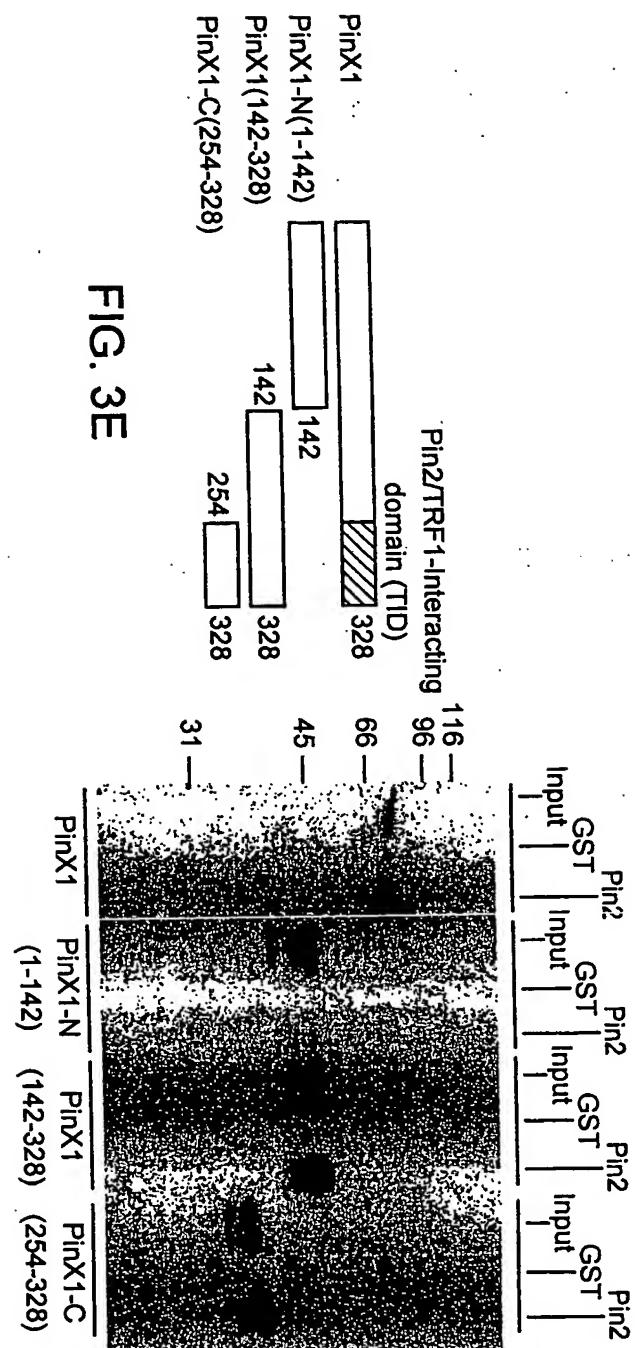


FIG. 3E

FIG. 3F

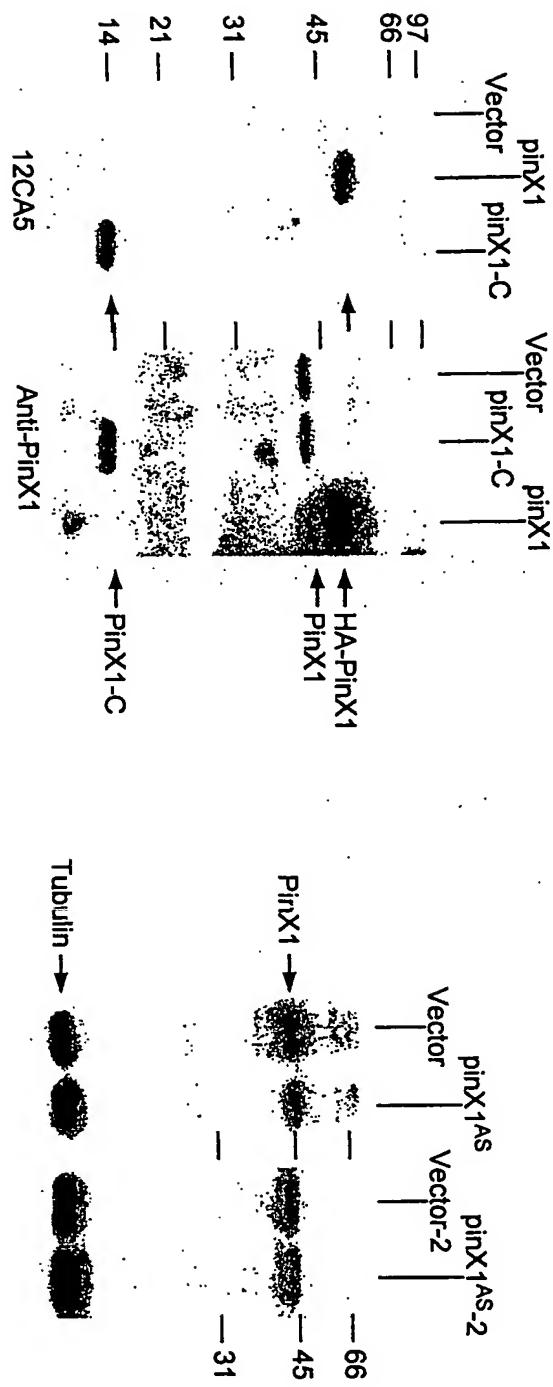


FIG. 4A

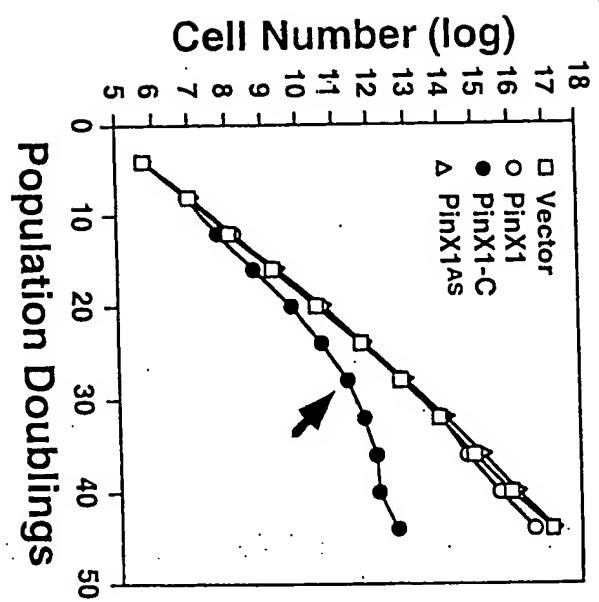


FIG. 4C

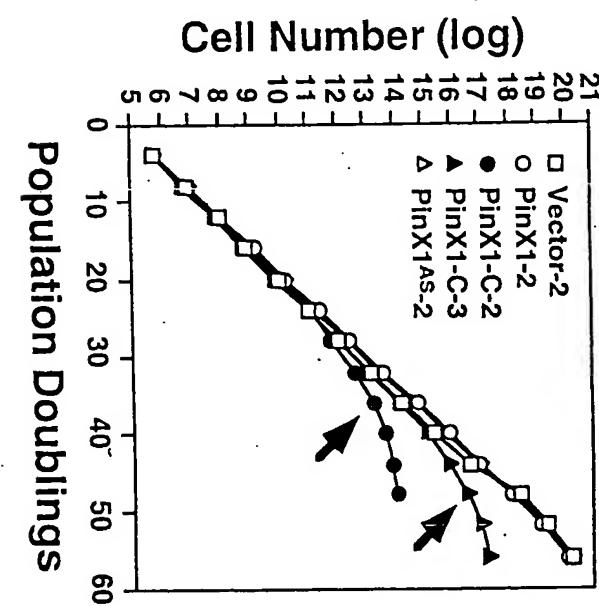
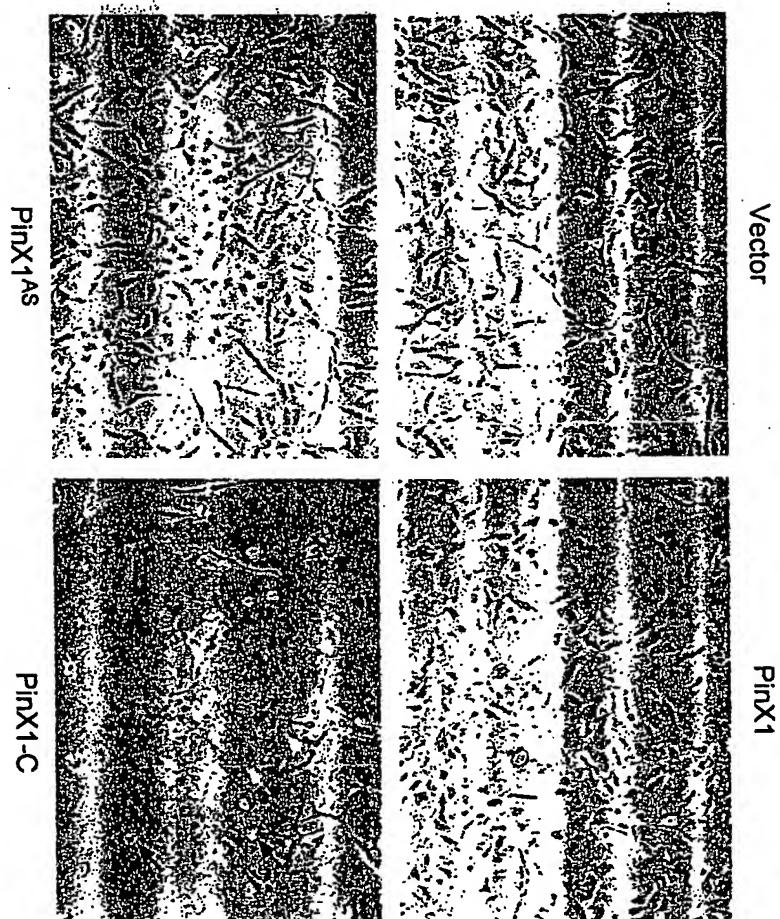
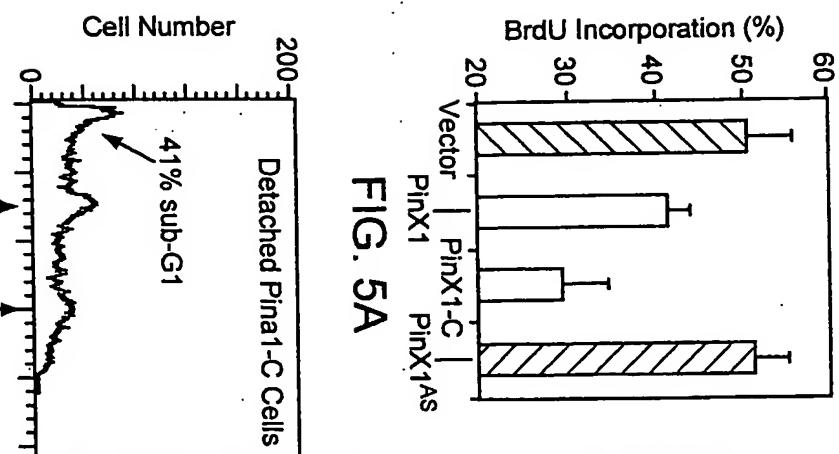


FIG. 4D



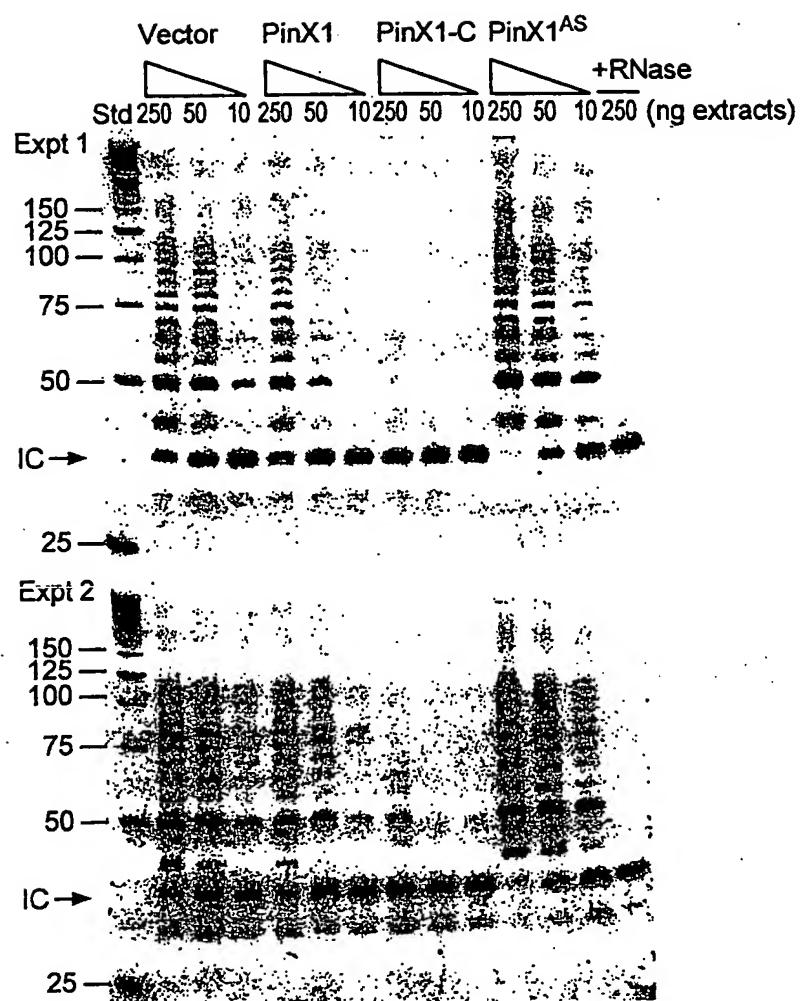


FIG. 6A

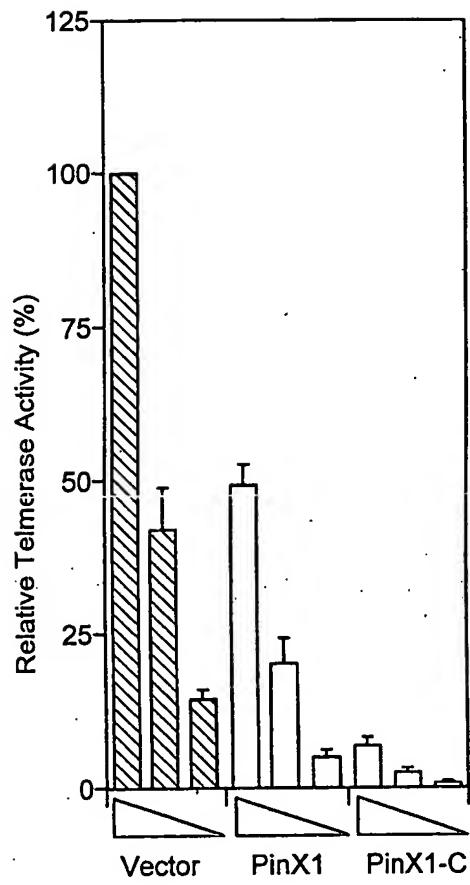


FIG. 6B-1

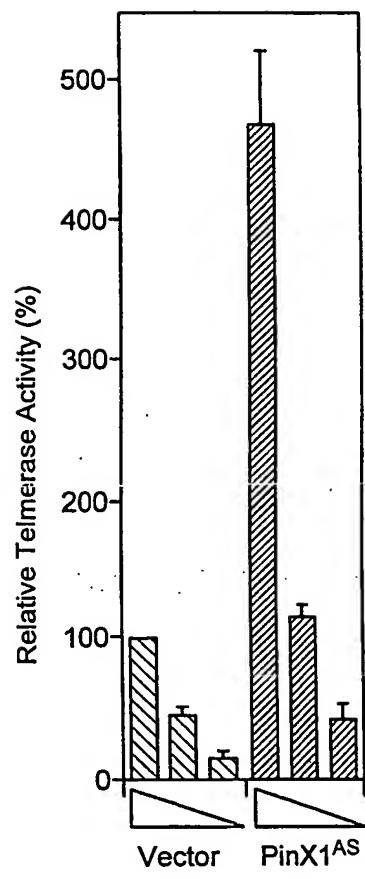


FIG. 6B-2

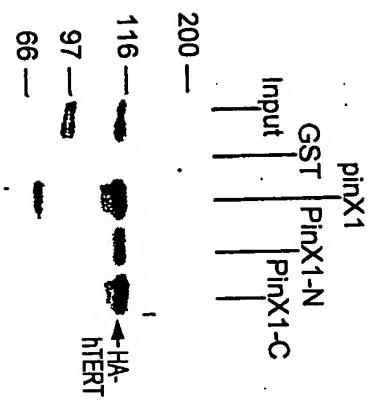


FIG. 7A

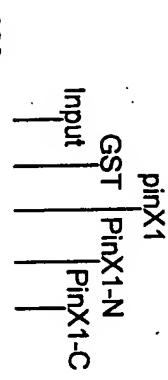


FIG. 7B

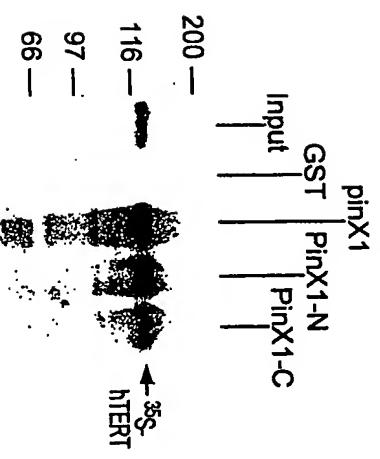


FIG. 7C

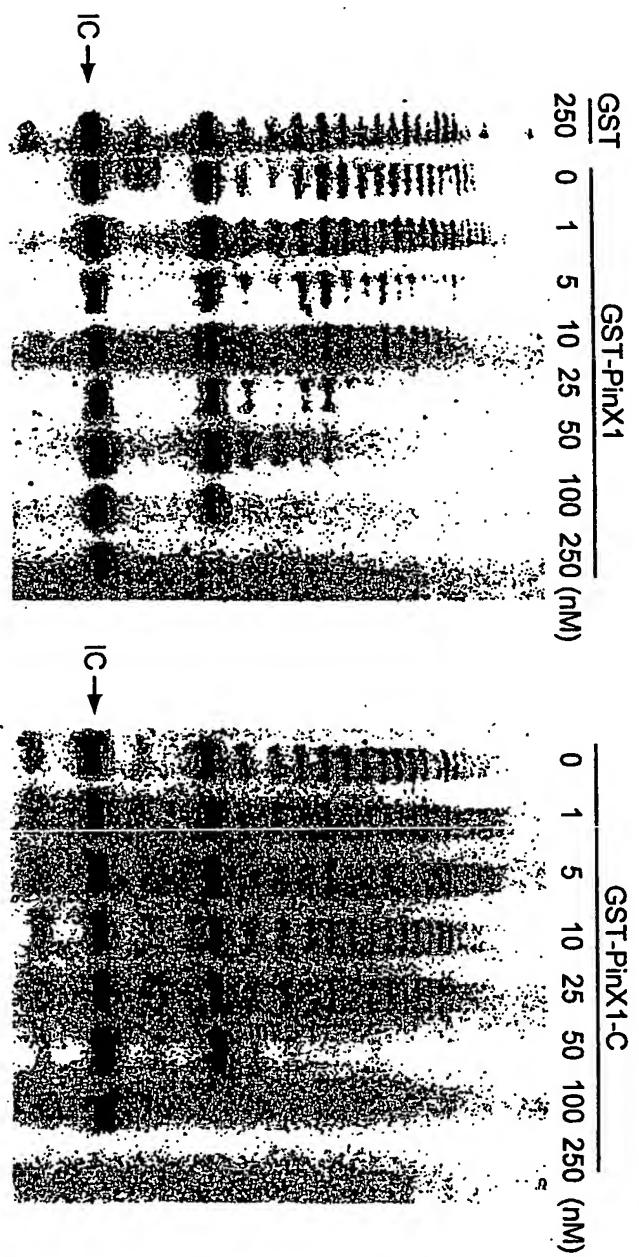


FIG. 7E

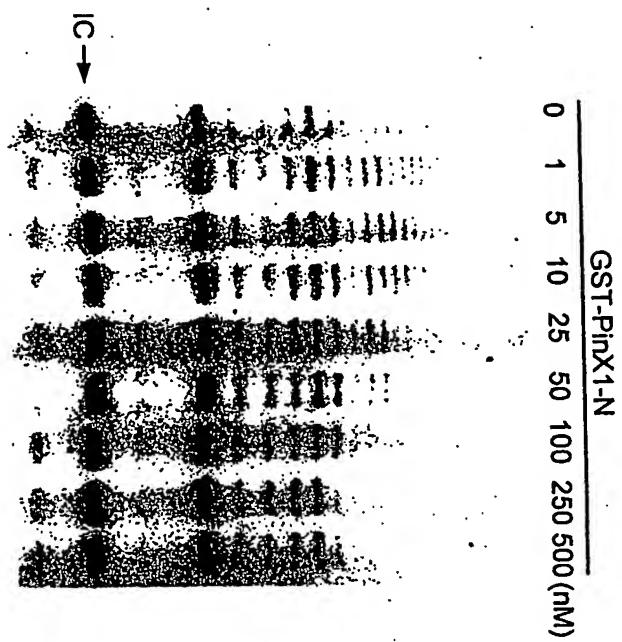


FIG. 7F

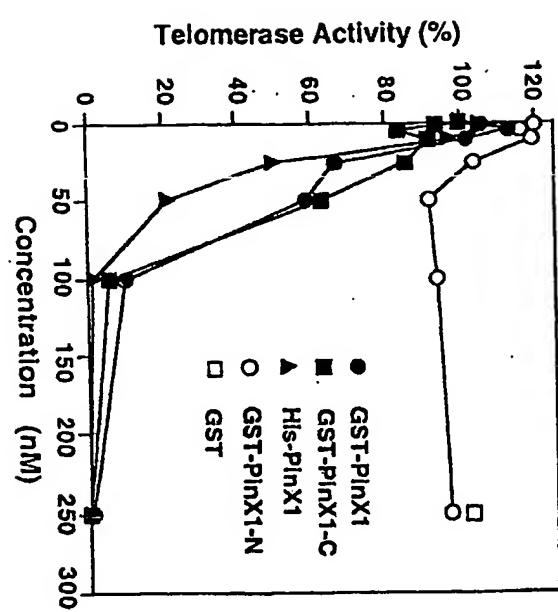


FIG. 7G

Table 1. Functional Properties of Pinx1 and its Mutants

Pinx1 Protein	Pin2/TRF1 Binding	hTERT Binding	Inhibition on Telomerase in vitro	Effect on Telomerase in Cells	Effect on Cell Growth in vivo
Pinx1	1  T1D	+	+	Partially inhibit	Partially inhibit
Pinx1-N	1  T1D	-	+	N.D.	N.D.
Pinx1-C (T1D)	254  T1D	+	+	Completely inhibit	Induce crisis
Pinx1AS "328"	 "1"	N.A.	N.A.	Increase	No affect

FIG. 8

Expression of PinX1 is decreased in some human
tumor tissues as determined by immunostaining

Tissues	PinX1 Expression	
	Normal	Tumor
Liver	+	-
Breast	+	-
Kidney	+	-
Skin	+	-
Colon	+	-

FIG. 9

Depletion of PinX1 by expression of antisense PinX1 increases the tumorigenicity of HT1080 cells

HT1080 cell lines	Tumor Frequency	Tumor Weight (g)
Vector	2/5	0.05, 0.01
PinX1 ^{AS}	4/5	0.6, 1.0, 1.2, 3.5
PinX1	0/5	
PinX1-C	0/5	

FIG.10A

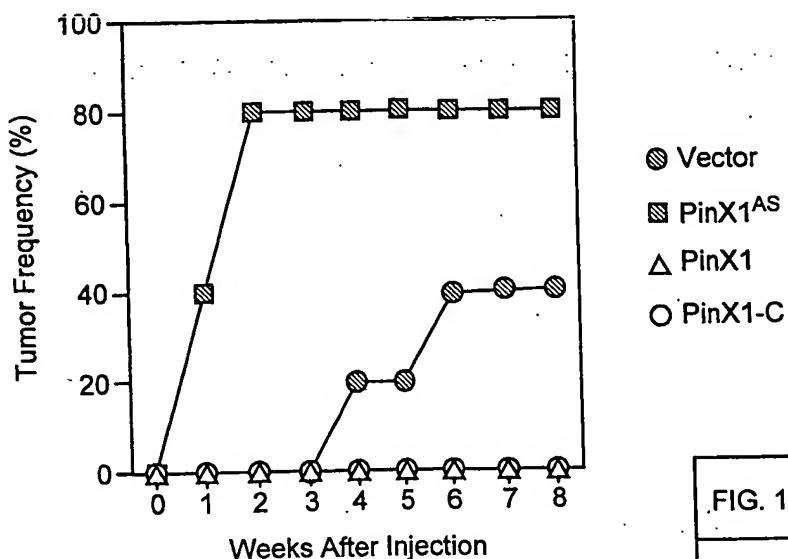


FIG.10B

FIG. 11A
FIG. 11B

FIG. 11

PinX1-L1 cDNA sequence (needed to be finally confirmed)

ATGTTGATGCTGGCTGAGCAGCAGGAAGCAGAAGTGGGCTGTGAATACTCAAACACTG
CCTGGAGTAATGCTGATTCTAAATTGGCCAGAGGATACTAGAGAAGATGGAATGGTCTAA
GGAAGGGTTAGGGGTCAGGAGCAAGGAGGCCAGATGATTAAGTTCAAGTTAA
ATAACGACCTGGGACTTCAAGCTACAATCAATAATGAAGCCAACGGATGCCCATCAAGAT
GATTTAACTGGCTCTGGGGAACTGAACACTGTGAGGGAGGAACAGCAGACTCCTT
AGACAACAGAAAAAGAAATATTAGTCTGAAGAAATTCAAATCTCAAAACTGTGTT
CATCATAGGAAATTACAAAAGAAAAGGATCTCATCTCGGAGCAAAACAGATCGTGACTG
CATTTTGGGAAACACGGATGACCAACCCATGCCTCACCATCCAGGGAGCTGACATTCCAAGACCA
ACAAGAACAAACCGACCAAGCCCCAGGTTGCACTCCAGGGCTGACATTCCAAGACCA
ATGGCAGCACTGAAGAACAAAGGCCAGGAGCTGAGGAGCTAAGAGACTCCGAGGGTAATTCCAGTCCCTCCACTCAG
AAGTGGAAATGCAAAGGGGAAGAAAAGAACAAAGAGGCAACAGGTAATAATGGGAGAG
TTACCCCCAACACAGCTAAGGCCAAGCGGCCAAAGAGGGAAAGCCTAAGAGAGACAG
GTCAGAAGTGGCATCCAAGGAGAAAGAGGACACGGACAGGACAGCAGAGGCC
TGCTGGGAAGAGAGTTCTGAGGCCTCTGCTCAGGGTGCAGGGATTGTTGCAAGGCCACCTG
ATGGCCAGGATTTCACCCCTGAAGGCCAAAAGACAAGAGGAAAAAAAGCTGCAAGCC
AGTAGAGGGTAGCAATGGACACTACGCTGAAGAACACCAATGAAAATAAGAAAAGAAGA
AAGGTTCCAATGAATTCTCCAGCCAGGGCCTCCGACCACCTCAGCTTGTCAAGGGGCT
GCTGGGGCAGACACCTCTGGCCTGAAGTCAGAGCAGAGTTCAACCCAGAGAGGGGGGCA
CATCTGTGACATGCCTGTGGGGAGTCTCGCCCTCACCCACATTCTCCCCAAGTT
ATGTTCCCAGGGGCTTTTTAAATGTTCTAAATCATGGCTTCAAAACAAATACATT
GTAA

FIG. 11A

PinX1-L1 peptide sequence (needed to be finally confirmed)

MLMLAEGQQKAKWAVNTQNTAWSNADSKFGQRILEKMEWSKGRLGVQEQQGPDDIKVQK
NNDLGLQATINNEANWIAHQDDFNWLLELNTCQRQETADSLDNKKKKYFSLEEIFKSSKNCVH
HRKFTKEKDLSRSKTDRCIFGKKQSKTPEGNSSPSTPDKNKTTMTHAFTIQERFAKRMAL
KNKPQVAAPGPDISKTOVECKRGKKRNKEATGKNGESYRPTAPKAKRPKEGKPKRDKVQKSAS
KEKRARTDGQCRCGLCWEESESEAQAQGAGNCVQPPDGQDFTLKPKKTRGKKKAQKPVEMDT
TLKETPMKNKKKKGSK

FIG. 11B

Alignment Report of Untitled, using J. Hein method with PAM250 residue weight table.

Thursday, May 3, 2001 11:42 AM

		Consensus #1			
		10	20	30	40
1	M S M L A E R R K Q K W A V D P Q N T A W S N D D S K F G Q R . L E K M . W S				
1	M L M L A E Q Q Q K Q K W A V N T Q N T A W S N A D S K F G Q R I L E K M E W S				
	K G . G L G . Q E Q G . . D . I K V Q V K N N . L G L . A T I N N E . N W I A H				
		50	60	70	80
41	K G K G L G A Q E Q G A T D H I K V Q V K N N H L G L G A T I N N E D N W I A H				
41	K G R G L G V Q E Q G G P D D I K V Q V K N N D L G L Q A T I N N E A N W I A H				
	Q D D F N . L L A E L N T C . . Q E T . D S . D . K . K K . F S L E E . . K . S				
		90	100	110	120
81	Q D D F N Q L L A E L N T C H G Q E T T D S S D K K E K K S F S L E E K S K I S				
81	Q D D F N W L L A E L N T C Q R Q E T A D S L D N K K K Y F S L E E I P K S S				

FIG. 12A

FIG. 12B

FIG. 12C

FIG. 12A

FIG. 12

K N . V H . . K F T K . K D L S S R S K T D . D C I F G K . Q S K K T P E G . . Consensus #1
 130
 140
 150
 160
 121 K N R V H Y M K F T K G K D L S S R S K T D L D C I F G K R Q S K K T P E G D A Pimx1-aa
 121 K N C V H H R K F T K E K D L S S R S K T D R D C I F G K K Q S K K T P E G N S Pimx1-lla

S P S T P . . N . T T . T T . A F T I Q E . F A K . . A A L K N K P Q V . . P G Consensus #1
 170
 180
 190
 200
 161 S P S T P E E N E T T - T T S A F T I Q E Y F A K P V A A L K N K P Q V P V P G Pimx1-aa
 161 S P S T P D K N K T T M T T H A F T I Q E R F A K R M A A L K N K P Q V A A P G Pimx1-lla

. D I S . T Q V E . K R G K K R N K E A T G K . . E S Y . . Q P K A K R . . E Consensus #1
 210
 220
 230
 240
 200 S D I S E T Q V E R K R G K K R N K E A T G K D V E S Y - - L Q P K A K R H T E Pimx1-aa
 201 P D I S K T Q V E C K R G K K R N K E A T G K N G E S Y P P T Q P K A K R P K E Pimx1-lla

G K P . R . . . Q . . . K . K . A . . . Q . R G . C W . . S S . A S A Q . A Consensus #1
 250
 260
 270
 280
 238 G K P E R A E A Q E R V A K K C A P A E K Q L R G P C W D Q S S K A S A Q D A Pimx1-aa
 241 G K P K R D K V Q K S A S K E K R A R T D G Q C R G L C W E E S S E A S A Q G A Pimx1-lla

FIG. 12B

G . . V Q P P . G . D F T L K P K K . R G K K K . . K P V E . A . D . T L . E T Consensus #1
290
300
310
320
278 G D H V Q P P E G R D F T L K P K K R R G K K L Q K P V E I A E D A T I E E T Pimx1-aa ..
281 G N C V Q P P D G Q D F T L K P K K T R G K K K A A K P V E V A M D T T L K E T Pimx1-Llaa

... . K K K K K . S K

330

318 - L V K K K K K D S K
321 P M K N K K K K G S K

Consensus #1

Pimx1-aa
Pimx1-Llaa

Consensus 'Consensus #1': When all match the residue of the Consensus show the residue of
the Consensus, otherwise show ' '.

FIG. 12C

NCBI

Entrez Nucleotide

PubMed Nucleotide Protein Genome Structure PopSet Taxonomy OMIM

Search for

Display Default View as HTML Save Add to Clipboard

Limits Index History Clipboard

1: U74382 Human telomeric repeat PubMed, Protein, Related Sequences, Taxonomy, OMIM, LinkOut

U74382 DNA-binding protein (PIN2) mRNA, complete cds

LOCUS HSU74382 1929 bp mRNA PRI 30-SEP-1999
 DEFINITION Human telomeric repeat DNA-binding protein (PIN2) mRNA, complete
 cds.

ACCESSION U74382
 VERSION U74382.1
 KEYWORDS telomere protein; telomere maintenance; mitotic regulator; NIMA-interacting proteins (Pins); cell cycle regulation.

FIG. 13A

FIG. 13B

FIG. 13C

FIG. 13D

FIG. 13A

FIG. 13

SOURCE	human.
ORGANISM	<u>Homo sapiens</u>
REFERENCE	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
AUTHORS	1. (bases 1 to 1929) Lu, K.P., Hanes, S.D. and Hunter, T.
TITLE	A human peptidyl-prolyl isomerase essential for regulation of mitosis
JOURNAL	Nature 380 (6574), 544-547 (1996)
MEDLINE	<u>96195064</u>
REFERENCE	2. (bases 1 to 1929) Shen, M., Hagglom, C., Vogt, M., Hunter, T. and Lu, K.P.
AUTHORS	Characterization and cell cycle regulation of the related human
TITLE	telomeric proteins Pin2 and TRF1 suggest a role in mitosis
JOURNAL	Proc. Natl. Acad. Sci. U.S.A. 94 (25), 13618-13623 (1997)
MEDLINE	<u>98054283</u>
PUBMED	<u>9391075</u>
REFERENCE	3. (bases 1 to 1929) Lu, K.P. and Hunter, T.
AUTHORS	Direct Submission
TITLE	Submitted (15-OCT-1996) Molecular Biology and Virology Laboratory,
JOURNAL	Salk Institute, 10010 North Torrey Pines Rd, La Jolla, CA 92037, USA
FEATURES	Location/Qualifiers
source	1..1929 /organism="Homo sapiens" /db_xref="taxon:9606" /cell_line="HeLa" 1..1929 /gene="PIN2"
gene	

FIG. 13B

CDS

1..1260
/gene="PIN2"
/note="NIMA-interacting protein 2, a potential coordinator
between mitotic progression and telomere homeostasis"
/codon_start=1
/product="telomeric repeat DNA-binding protein"
/protein_id="AAB53363_1"
/db_xref="GI:2058493"
/translation="MAEDVSSAAPSPPRCADGRDADPTEEQMAETERNDEEQFECQEL
LECQVQVGAPEEEEEEEDAGLYVAEAEAVAGWMLDFLCISICRAFRDGRSEDFRTR
NSAEAIHGSSLTACQLRTYICQLTRIAAGTQDAQFENDERITPESALMIWS
IEKEHDKHEEIQNLIKIQIAVCMENGNFKEAEFFERIFGDPNSHMPFKSLMII
SQKDTFHSSFOHSYNSHMEKISVNVYULSEKSSTFLMKAALKVUESKRTTITSQD
KRGSGNDVEMETEANLDTRKRSHKNLFLSKLQHGTQODDLNKKERRVGTPOSTKKES
RATESRIPVSKSQPVTPKHKRARKRQAWLWEEDKNLRLSGVRKYGEGNWNISKILLHYKE
NRRTSVMLKDRWRTMKKLKLISSDSD"

BASE COUNT
ORIGIN
618 a 386 c 435 g 490 t

1 atggggagg atgtttccg agcgccccg agcccgccg ggtgtgcgg a ggttaggt
61 gccgacccta ctgaggagca gatggcaga acagagagaa acgacgagga gca gcatgtcgaa
121 tgccaggaac tgctcgagtg ccaggtgcg gtggggccc ccaggagga ggaggagg
181 gaggaggacg cggcgcgtgt ggcgcggcc gaggccgtgg ctgcgcgcgtg gatgtcgat
241 ttccctgtcc tctctcttgc cggagcttc cgcgcacggc gctccgagga cttccgcagg
301 acccgcaaca ggcgcagagc tattattcat ggactatcca gtcataacagc ttgcgcgttg
361 agaacgatat acatatgtca gttttgaca agaattgcg caggaaaac ctttgatgca
421 cagtttgaaa atgtatgcgc aattacaccc ttggaatcag ccctgtatgtat ttgggtca
481 attgaaaagg aacatgacaa acttcatgaa gaaatacaga atttaattaa aattcaggct
541 atagctgttt gtatggaaa tggcaacttt aagaagcag aagaagtctt tgaagaata
601 ttttgtatc caaattctca tatgccttc aaaagcaat tgcttatgtat aatctctcag
661 aaagatatacat ttcatccctt ttcaacac ttcaatcaca accacatgat ggagaaaatt
721 aagagttatg tgaattatgt gctaagtggaa aatcatcaa ctttcttaat gaaggcagcg
781 gcaaaatgtt tagaaagcaa aaggacaaga acaataactt ctcagaataa accttagtgg

FIG. 13C

841 aatgatgttg aatggaaac tgaagcta at ttggatacaa gaaaaggc tcacaagaat
901 cttttcttat ctaagttgca acatggaaac cagcaacaa ag ccttaataa gaaaaga
961 agatggaa ctcctcaaaag tacaaaaag aaaaagaa gcaagaagc cactgaaagc
1021 agaataacctg ttcaaaagag tcagccgta actcctgaaa aacatcgac tagaaaaga
1081 caggcatggc ttggaaaga agacaagaat ttgagatctg gcgtgaggaa atatggag
1141 ggaacttgt ctaaaatact gttgcattt aaattcaaca accggacaag tgcata
1201 aaagacagat ggaggaccat gaagaaacta aactgtatt cctcagacag cgaagactga
1261 ttgtgtttgt aaaagcttga tgaaggaca gttaaagtatt ttgatcactg cattttgtt
1321 gaaacttgt tcattgtt aatttaaac ttttttttaa agcattacag tattttctg
1381 tgaccatcaa ttatgaggg tttgtgtcac cagatgtaaa gcatatgtca tcattgtt
1441 ctttaagaac ctatatttga taaaatgtaa attttgttga ccttgcaca ttttagtatcc
1501 ccaccccaa atctgttcc aatggaaaaa ttaaaacctg atacggaaaa aaaaaaattc
1561 cagtttaaccc tttttgttgc tttttgttgc cttcaacccct gtaacgttaac ccattaaat
1621 gaattttttt ttttttaaga cagatgttct ctctgttgcc caggtggag tgcagtggcg
1681 caatttcagc tcactgttcc aggtcaagtq attttccctgc ctcagccct
1741 gatgtgttgc gattacaggc acacaccacc agccagctaa tttttgtatt tttagtag
1801 gccccgttcc accatgttgc tcaggatgtt ctccaaactcc tgacttcatg atccacccac
1861 ctccggcctcc caaagtgttgc agattacaga cgtgagccac tgcgtccctgc ctaaaatgaa
1921 tttttctaga

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FIG. 13D